PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Artcle 36 and Rule 70)

Applicant's or agent's file reference OP03-0149	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. **PCT/KR2004/000251**	International filing date *(day/month/year)* **09 FEBRUARY 2004 (09.02.2004)**	Priority date *(day/month/year)* 26 NOVEMBER 2003 (26.11.2003)

International Patent Classification (IPC) or national classification and IPC

A61K 36/489(2006.01)i, A23L 1/29(2006.01)i, A61P 19/00(2006.01)i

Applicant

REXGENEBIOTECH CO., LTD. et al

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ (sent to the applicant and to the International Bureau) a total of 4 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
   - ☒ Box No. I Basis of the report
   - ☐ Box No. II Priority
   - ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☐ Box No. VIII Certain observations on the international application

Date of submission of the demamd	Date of completion of this report
26 SEPTEMBER 2005 (26.09.2005)	08 MARCH 2006 (08.03.2006)
Name and mailing address of the IPEA/KR Korean Intellectual Property Office 920 Dunsan-dong, Seo-gu, Daejeon 302-701, Republic of Korea Facsimile No. 82-42-472-7140	Authorized officer YEO, Ho Sup Telephone No. 82-42-481-5627

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/KR2004/000251

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language _____,
   which is the language of a translation furnished for the purposes of:

   ☐ international search (under Rules 12.3 and 23.1(b))
   ☐ publication of the international application (under Rule 12.4)
   ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this reort as "originally filed" and are not annexed to this report):*

   ☐ the international application as originally filed/furnished

   ☒ the description:
   pages 1-53 as originally filed/furnished
   pages* _____ received by this Authority on _____
   pages* _____ received by this Authority on _____

   ☒ the claims:
   pages _____ as originally filed/furnished
   pages* _____ as amended (together with any statment) under Article 19
   pages* 54-57 received by this Authority on 26/09/2005
   pages* _____ received by this Authority on _____

   ☒ the drawings:
   pages 1/21-21/21 as originally filed/furnished
   pages* _____ received by this Authority on _____
   pages* _____ received by this Authority on _____

   ☒ the sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☒ The amendments have resulted in the cancellation of:

   ☐ the description, pages _____
   ☒ the claims, Nos. 9, 14
   ☐ the drawings, sheets _____
   ☐ the sequence listing *(specify)* : _____
   ☐ any table(s) related to sequence listing *(specify)* : _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

   ☐ the description, pages _____
   ☐ the claims, Nos. _____
   ☐ the drawings, sheets _____
   ☐ the sequence listing *(specify)*: _____
   ☐ any table(s) related to sequence listing *(specify)* : _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 7, 8, 10-13

because:

☒ the said international application, or the said claims Nos. 7, 8, 10-13 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

The subject-matter of claims 7, 8 and 10-13 does not require an international preliminary examination with respect to industrial applicability, as it is directed to a method for treatment of the human or animal body by therapy (PCT Article 34(4)(a)(i) and Rule 67.1(iv)).

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*:

☐ no international search report has been established for said claims Nos. _____.

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Istructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.
- ☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Istructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.
- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13ter.1(a) or (b) and 13ter.2.

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the techmical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-6, 15	YES
	Claims		NO
Inventive step (IS)	Claims	1-6, 15	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-6, 15	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

The present invention relates to a composition for preventing or treating metabolic bone disease, comprising a hot water extract of Sophorae Fructus as an active ingredient.

The following documents have been considered for the purpose of this report :

D1 = US 2003/0180394 A1 (25. 09. 2003)
D2 = KR 2002-0044745 A (19. 06. 2002)

D1 states that the extracts of roots of Sophora species are effective for the prophylaxis and therapy of pathological conditions caused by estrogen deficiency, in particular osteoporosis.

D2 states that an extract of Sophorae Flos contains a large amount of phytoestrogen and can be used as a therapeutic agent for osteoporosis.

Even though D1 and D2 are relevant to the present invention, none of them teach or fairly suggest that a hot water extract of Sophorae Fructus would be useful for preventing or treating metabolic bone disease.

As a consequence, claims 1-6 and 15 meet the criteria set out in PCT Article 33(2)-(4).

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Supplemental Box Relating to Sequence Listing

Continuation of Box No. I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:

   a. type of material
      - ☒ a sequence listing
      - ☐ table(s) related to the sequence listing

   b. format of material
      - ☒ on paper
      - ☒ in electronic form

   c. time of filing/furnishing
      - ☒ contained in the international application as filed
      - ☒ filed together with the international application in electronic form
      - ☐ furnished subsequently to this Authority for the purposes of search and/or examination
      - ☐ received by this Authority as an amendment* on _____

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed of furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

WHAT IS CLAIMED IS:

1. (Amended) A pharmaceutical composition for preventing or treating metabolic bone disease comprising a hot water extract of *Sophorae Fructus* as an effective ingredient.

2. (Amended) The pharmaceutical composition of claim 1, wherein said hot water extract of *Sophorae Fructus* is prepared by the steps of:

(a) adding water to the *Sophorae Fructus* powder, wherein the amount of water is 3 to 20 times as much as the weight of *Sophorae Fructus* powder; and

(b) hydrothermal extracting the composition of step (a) for 1 to 6 hours to obtain the hot water extract of *Sophorae Fructus*.

3. (Amended) The pharmaceutical composition of claim 1, wherein said hot water extract of *Sophorae Fructus* is prepared by the steps of:

(a) adding water to the *Sophorae Fructus* powder, wherein the amount of water is 3 to 20 times as much as the weight of *Sophorae Fructus* powder;

(b) hydrothermal extracting the composition of step (a) for 1 to 6 hours to obtain the hot water extract of *Sophorae Fructus*; and

(c) adding amylase or pectinase to the hot water extract of *Sophorae Fructus* of the step (b) by 0.01 ~ 1%(v/v), and reacting for 4 ~ 24 hours.

4. (Amended) The pharmaceutical composition of claim 1, wherein the

AMENDED SHEET

metabolic bone disease is selected from the group consisting of osteoporosis, lumbago, rheumatoid arthritis, degenerative arthritis, rickets, osteomalacia and Paget's disease of bone.

5. (Amended) A food composition for preventing or improving metabolic bone disease comprising a hot water extract of *Sophorae Fructus* as an effective ingredient.

6. (Amended) The food composition of claim 5, wherein the metabolic bone disease is selected from the group consisting of osteoporosis, lumbago, rheumatoid arthritis, degenerative arthritis, rickets, osteomalacia and Paget's disease of bone.

7. (Amended) A method of preventing or treating metabolic bone disease, which comprises administering a pharmaceutical composition comprising a hot water extract of *Sophorae Fructus* to a subject.

8. (Amended) The method of claim 7, wherein the metabolic bone disease is selected from the group consisting of osteoporosis, lumbago, rheumatoid arthritis, degenerative arthritis, rickets, osteomalacia and Paget's disease of bone.

9. (Cancelled)

10. (Amended) The method of claim 7, wherein the metabolic bone disease is prevented or treated by stimulating the osteoblast proliferation, the secretion of a

growth factor involved in bone reformation, and the generation of nitric oxide in the osteoblast by the administration of the pharmaceutical composition comprising the hot water extract of *Sophorae Fructus* to a subject.

11. The method of claim 10, wherein the growth factor involved in bone reformation is IGF-1 or TGF-β.

12. (Amended) The method of claim 7, wherein the metabolic bone disease is prevented or treated by inhibiting the secretion of bone-absorptive cytokines or the osteoclast differentiation by the administration of the pharmaceutical composition comprising the hot water extract of *Sophorae Fructus* to a subject.

13. The method of claim 12, wherein the bone-absorptive cytokine is IL-1 beta or IL-6.

14. (Cancelled)

15. (Amended) Use of a hot water extract of *Sophorae Fructus* for the preparation of a medicament for preventing or treating metabolic bone disease.

AMENDED SHEET

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WHAT IS CLAIMED IS:

1. (Amended) A pharmaceutical composition for preventing or treating metabolic bone disease comprising a hot water extract of *Sophorae Fructus* as an effective ingredient.

2. (Amended) The pharmaceutical composition of claim 1, wherein said hot water extract of *Sophorae Fructus* is prepared by the steps of:

(a) adding water to the *Sophorae Fructus* powder, wherein the amount of water is 3 to 20 times as much as the weight of *Sophorae Fructus* powder; and

(b) hydrothermal extracting the composition of step (a) for 1 to 6 hours to obtain the hot water extract of *Sophorae Fructus*.

3. (Amended) The pharmaceutical composition of claim 1, wherein said hot water extract of *Sophorae Fructus* is prepared by the steps of:

(a) adding water to the *Sophorae Fructus* powder, wherein the amount of water is 3 to 20 times as much as the weight of *Sophorae Fructus* powder;

(b) hydrothermal extracting the composition of step (a) for 1 to 6 hours to obtain the hot water extract of *Sophorae Fructus*; and

(c) adding amylase or pectinase to the hot water extract of *Sophorae Fructus* of the step (b) by 0.01 ~ 1%(v/v), and reacting for 4 ~ 24 hours.

4. (Amended) The pharmaceutical composition of claim 1, wherein the

metabolic bone disease is selected from the group consisting of osteoporosis, lumbago, rheumatoid arthritis, degenerative arthritis, rickets, osteomalacia and Paget's disease of bone.

5. (Amended) A food composition for preventing or improving metabolic bone disease comprising a hot water extract of *Sophorae Fructus* as an effective ingredient.

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growth factor involved in bone reformation, and the generation of nitric oxide in the osteoblast by the administration of the pharmaceutical composition comprising the hot water extract of *Sophorae Fructus* to a subject.

11. The method of claim 10, wherein the growth factor involved in bone reformation is IGF-1 or TGF-β.

12. (Amended) The method of claim 7, wherein the metabolic bone disease is prevented or treated by inhibiting the secretion of bone-absorptive cytokines or the osteoclast differentiation by the administration of the pharmaceutical composition comprising the hot water extract of *Sophorae Fructus* to a subject.

13. The method of claim 12, wherein the bone-absorptive cytokine is IL-1 beta or IL-6.

14. (Cancelled)

15. (Amended) Use of a hot water extract of *Sophorae Fructus* for the preparation of a medicament for preventing or treating metabolic bone disease.

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